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/Following is the translation of an article by Irzhi Shonka (Prague) entitled "O Klinicheskom Znachenii Pentozovogo Tsikla" (English version above) in Klinicheskaya Meditsina (Clinical Medicine), Vol. 38, No. 7, July 60, pages 3-12./

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Although only a few years have passed since the discovery of the pentose cycle, today, all issues of biochemical journals contain one or more works devoted to this problem. At first, even the biochemists thought that the pentose cycle was a freak of nature characteristic of only a few microorganisms, and of no significance; however, it has turned out that this cycle is observed in tissues of a great variety of organisms. It was further elicited that although the pentose cycle from the point of view of the amount of glucose metaboliczed, is insignificant as compared with anaerobic glycolysis, nevertheless it has great importance in pathology.

Heretofore, medical opinion has ignored this discovery in seeking solutions of corresponding problems. This neglect is due in part to the negative attitude of some medical biochemical laboratories which do not recognize the existence of the pentose cycle in mammalian tissues. For instance, at the Cardiological Conference in Garakhovo (June 1958), where new trends in the study of the pentose cycle should have been dealt with, these were considered not of vital importance. We are of the opinion that it is precisely at such conferences that a study of new trends should be discussed and that discussion should not be limited to the repetition of long-known facts described in textbooks.

Biochemical data

In this review we shall not dwell in detail on biochemical processes, but only point out the essence of glucose metabolism.

After the requisite initial phosphorylation of glucose on the sixth atom of carbon, the splitting of glucose can proceed in two ways: via known anaerobic glycolysis (according to Embden, Meyerhof, Parnas and via oxidation. The name for the latter, new way of glucose splitting has not yet been established, and in the literature we come across such terms as "direct oxidation process." "shortened oxidation of glucose" (shunt), "decarboxylating oxidation of glucose-6-phosphate," "oxidation cycle of glucose-6-phosphate," "pentose cycle," etc.). We employ the last designation, since it conveys well the essence of the process. The glucose-6-phosphate is oxidized by dehydrogenase into gluconо-6-phosphate, which in turn undergoes further oxidation under the influence of another dehydrogenase into a 3- or 2-keto-glucono-6-phosphate; simultaneously, a spontaneous decarboxylation of ketogluconophosphate on C_1 takes place, and the isomerization leads to the formation of pentoses, riboso-ribuleso- and xylulose-5-phosphate. The coenzyme of both dehydrogenases is triphosphopyridine nucleotide (TPN), which is deoxidized to TPNH.

During further stages, a rearrangement of remnants of the two pentose-phosphate molecules takes place in such a way as to form a glucose-6-phosphate which is again decarboxylated by the two aforementioned dehydrogenases. The corresponding enzymes are transaldolase and transketolase. Schematically, this gradual oxidation of residues of pentose-phosphates appears as follows:

$$5C + 5C \longrightarrow 7C + 3C$$

$$7C + 3C \longrightarrow 4C + 6C \xrightarrow{\uparrow CO_2} 4C + 5C$$

$$4C + 5C \longrightarrow 3C + 6C \xrightarrow{\uparrow CO_2} 3C + 5C$$

Thus, in addition to triosephosphate, there are formed sugars heretofore uncommon in the biochemistry of mammals, that are characterized by seven carbon atoms (sedoheptuleso-phosphates) and four carbon atoms (erythrosophosphates). In our previous work the problems of the biochemistry of the pentose cycle were analyzed in more detail (Sonka, Cernoch).

Role of the pentose cycle in the dynamics of the organism

The question of the role in the utilization of glucose

played by the pentose cycle has interested biochemists for several years. In the first works relating to this subject, published in 1955-1956 (Wenner, Bloom, Bernstein), it was calculated, on the basis of studies of labeled glucose-6-phosphate on the first, second and sixth atoms of carbon, that 50 percent of glucose utilized in rat's liver is oxidized through the pentose cycle. At the beginning of 1956, by means of perfected methods of calculation and the use of more complex methods, it was demonstrated that seven to ten percent of the oxidation is accomplished by the pentose cycle (Ashmore, Katz, Wenner).

If we study the fate of labeled glucose in the organism not only from the points of view of oxidation and CO_2 formation but also as to its inclusion in other types of molecules, it becomes evident that, out of 100 glucose molecules, two are oxidized through the pentose cycle, 18 are included in glycogen, 55 are hydrolyzed up to glucose and enter the blood stream, and 25 are destroyed through anaerobic glycolysis (Sonka). Such a small role of the pentose cycle in glucose metabolism does not, however, diminish the significance of this process. Undoubtedly, the main sources of energy in glucose metabolism are anaerobic glycolysis and CKC; however, the pentose cycle, as we shall see later, fulfills special tasks. Furthermore, the enzyme activity of the pentose cycle under physiological conditions is not uniform in various tissues, and it is subjected to the influence of various activators and inhibitors in the same tissue. It is significant, for instance, that the enzyme activity of the pentose cycle (in relation to the total utilization of glucose by corresponding tissues) is almost zero in the skeletal musculature, and in the brain, it is insignificant (Glock, A. P. Barkhash and M. Ya. Timofeyeva) or zero (Wenner), whereas myocardium (Rudolph and Olsen) possesses pentose cycle activity analogous to that of the liver (Wenner, Glock and Kelly), kidneys (Wenner), retina, crystalline lens (V. A.Engel'gardt and A. P. Barkhash). The highest activity was observed in certain genital organs (Rudolph and Olsen) and especially in the lymphatic tissue and thymus (Kit, Wenner), suprarenal cortex (Kelly, Glock), and in the ovary and mammary gland during lactation (Glock).

Hormones and endocrinopathology

1. Glucocorticoids and ACTH. In some of our works we called attention to the increased activity of the pentose cycle in the erythrocytes of patients with surgical traumas, myocardial infarct, pulmonary infarct, etc. (Sonka, Dubovsky, Palek). We observed also an increased activity of the pentose

cycle in the erythrocytes of rats with advanced anoxia (Kopecky) and in erythrocytes of schizophrenic patients during a hypoglycemic coma (Palek). It was assumed that we were dealing here with a nonspecific activization of the suprarenal cortex which could influence the pentose cycle of glucocorticoid formation. It turned out, however, that the use of cortisone in vivo has no effect on the pentose cycle, whereas ACTH employed in vivo causes a marked increase of activity in the intact incubated cells; hemolysates and homogenates do not react to ACTH (Sonke, Kalousek, Dubovsky, Palek). These results correspond to the fact that ACTH activates phosphorylase in the suprarenal cortex only in whole organs or sections, and bot in homcgenates (Drew). It is also stated in that work that the biosynthesis of glucocorticoids is possible only through 11-hydroxylase, the coenzyme of which is TPNH; TPN, in a reduced form, maintains the pentose cycle activity, as is proved by the high activity of the pentose cycle in the suprarenal cortex (Kelly).

Thus, ACTH changes the phosphorylase activity of the suprarenal glands as well as the activity of other enzymes and, most probably, it influences both dehydrogenases of the pentose cycle; this effect occurs not only in the suprarenal cortex but, to a certain extent, in some other tissues as well (erythrocytes). Researchers who proceeded from analogous premises but worked with homogenates (Glock, Rudolph) did not observe the activating effect of ACTH on the pentose cycle.

2. Thyroxin. In vivo thyroxin causes activation of anaerobic glycolysis and the pentose cycle in liver homogenates (Glock) and in rat erythrocytes (Palek). In patients with thyrotoxicosis there was observed an increased activity of the pentose cycle in erythrocytes. It is important to note that TPNH is essential for the transformation of phenylalanine into tyrosine. This means that the pentose cycle influences the formation of thyroxin (Wolin). The use of methylthiouracil led to the normalization of the pentose cycle.

3. Estrogens and androgens. Estrogens and androgens had no effect on the pentose-cycle activity either in women during the post-climacteric period (Palek), or in male rats undergoing castration (Dubovsky). In contrast to this, Rudolph and Olsen think that estrogens and androgens exert an indirect activating influence on the pentose cycle.

4. Physiological and pathological growth (tumors). Fast-growing tissues utilize a large quantity of nucleotides. Ribose for ribonucleic acid comes from the pentose cycle; desoxyribose, on the contrary, is formed first of all in the synthesis of 2C and 3C fragments of glucose (G. A. Kritskiy). However, Bernstein noted in an experiment on chicks that ribose for fibonucleotides is formed apparently via synthesis of

glucose fragments rather than from decarboxylation of glucose. Indeed, it has been proved that the younger the tissues, the more pronounced is the activity of the pentose cycle. This is illustrated by the work of Kral who studied the pentose cycle. This is illustrated by the work of Kral who studied the pentose cycle activity in the growing eggs of a sea urchin and demonstrated that, as differentiation progressed, there was a gradual decrease in the amount of glucose affected by the pentose cycle, down to an amount characteristic for an adult organism. Analogous phenomena are observed also in regenerating tissues (Touster). It is necessary to note that in plants, in contrast, the pentose cycle plays a secondary role in meristems where growth is most intense, and that the cycle is observed only in differentiated plant tissues (G. A. Kritskiy), primarily in the so-called preclimacteric phase of fruit ripening.

The activity of the pentose cycle enzymes can be proved to increase also during the malignant growth of tissues. In this connection it is necessary first to recall the work of Manks, whose methods, however, were not satisfactory. On two occasions we studied this problem, and found that the erythrocytes of cancer patients (with the exception of bronchogenic cancer patients) form from glucose an increased amount of ribose, as well as sedohentulose. Our data confirmed other work which demonstrated a higher activity of the pentose cycle directly in the homogenates of various experimental tumors of rats (Villakicencio, Kit, Wenner, Abraham, G. A. Kritskiy).

The abnormal metabolism in cancer and leukemia patients is observed also in cells not connected with the tumor (erythrocytes); hence we are dealing here with either a humoral regulator (ACTH load) or a metabolic change caused by the effect of the carcinogenic virus on the organism; it is known that some forms of viruses and bacteriophages can inhibit glycolysis in bacteria, and thus indirectly stimulate the pentose cycle (Cohen). Bacteria affected by the virus are compelled to produce another type of nucleotide than the one they need. For example, E. coli, affected by a bacteriophage, produces ribonucleotides characteristic of the bacteriophage, instead of desoxyribonucleotides. Another factor increasing the pentose cycle activity in cancer patients could be the considerable need for ribose for the rapid formation of ribonucleic acid.

The effect of cytostatic substances has been utilized up to the present only from the point of view of blocking the synthesis of the purine or pyrimidine nucleus of the nucleotides; however, it has not yet been determined whether these substances exert an inhibiting effect also on the process of

formation of ribose from desoxyribose, the other component of nucleotides.

A more active pentose cycle in tumor tissue could also explain the Pasteur effect (Sonka).

5. Insulin. Insulin in vitro does not affect the pentose cycle in erythrocytes; in vivo administration of 20 units of insulin to healthy individuals also has no effect on the activity of the pentose cycle in erythrocytes; however, administration of 100 to 140 units of insulin to schizophrenic patients considerably activates the pentose cycle in erythrocytes but not in hemolysates (see effect of ACTH). Antidiabetic sulfanilamide preparations, which in vitro and in vivo do not cause any marked hypoglycemia, do not affect rats (Palek). In elderly diabetic patients the activity of the pentose cycle in erythrocytes was normal or slightly diminished; in contrast, in young individuals in ketosis or even coma, pentose cycle activity was observed to increase (effect of ACTH).

Pentose cycle and liposynthesis

The processes of synthesis and disintegration of fatty acids were clarified by the discovery of the Linen cycle of fatty acids. Here, too, the pentose cycle acts as a regulator (Milstein, Touster Hollman), in changing within the medium the ratio of TPN to TPNH, which represents the coenzyme of the reaction acetate-crotonyl → CoA + TPNH → TPN + butyryl → CoA $\lessgtr$ fatty acids / cholesterin. If there is a predominance of TPNH in the medium (that is, if the pentose cycle is active a liposynthesis takes place; if there is a predominance of TPN the pentose cycle is inactive and the fats disintegrate. In corespondence with this discovery, Slivovski, working in our laboratory, detected an increased activity of the pentose cycle in the erythrocytes of obese women. We are investigating at present the effect of various methods of treatment of obesity on the activity of the pentose cycle. The discovery of nontoxic inhibitors of this cycle would open up a new path in the treatment of obesity; thus far, however, we have succeeded only in clarifying one of the causes of weight increase in hogs, following administration of antibiotics: some antibiotics notably terramycin and ambramycin) substantially increase the utilization of glucose in erythrocytes, mainly through the pentose cycle. Here we are dealing not with the destruction of the parasitic bacterial flora in the intestines, the effect usually ascribed to antibiotics, but with a nonspecific effect on the corresponding enzymic systems (Kohoutek). Sometimes this effect causes also a sudden increase of weight in patients who had been given antibiotics for some insignifi-

cant disease.

Muscular activity

We thought that marked muscular tension might serve as a load increasing the activity of the pentose cycle. It turned out, however, that skeletal muscles do not contain pentose cycle enzymes, and that the glucose is split in this instance exclusively by means of glycolysis. In the erythrocytes of horses after intense muscular exertion, and in those of rats compelled to swim, we observe a similar result, namely activization of glycolysis and depression of the pentose cycle. However, in track athletes we observed, in isolated cases, the reverse reaction (Kalousek). We pointed out in the discussion that the atypical biochemical reaction to muscular tension may represent either the result of over training or a manifestation of individual characteristics which do not favor the achievement of best athletic results without endangering the health of the record-seeker. We had great difficulty in finding athletes for this study.

Because of its importance, this work deserves to be continued by some institute of physical culture where a large number of athletes would be available for puncture of a vein following a standard athletic exertion.

CO_2 fixation in mammals

Inclusion of CO_2 within large molecules has been considered, until recently a unique characteristic of green plants (photosynthesis). It has been proved, however, that mammalian tissue also may contain CO_2 within the molecules. For example, experiments have demonstrated that C^{14}-Tagged bicarbonate /tagged CO_2?/ administered intravenously, appears in milk in molecules of sugar, amino acids and fat (Sonka). The Co_2 fixation takes place at the pentose-phosphate stage, so that actually we are dealing here with a reverse pentose cycle (Jacoby). In principle, photosynthesis proceeds along the same lines as the pentose cycle but in the opposite direction. In plants there is observed, in addition to anaerobic glycolysis, pentose cycle activity regulated similarly to that in animals. Thus, for example, we are unable to prove that the pentose cycle in meristems is manifested only in differentiated tissue (Stoppani). The rise of activity of the pentose cycle in fruits during the so-called preclimacteric phase is notable. The collected fruits lose their green color, become softer, and acquire their characteristic taste and flavor. At this stage there is an increase in utilization

of O_2 and elimination of CO_2. There is a temporary increase in pentose cycle activity which is explained by the fact that it is essential during the preclimacteric period for the synthesis of some substances characteristic of the ripe fruit. The pentose cycle is also needed for the maintenance of a correct ratio between L-ascorbic and dehydroascorbic acid in plants (Marre).

Chemotherapeutic substances

It is possible that some medicinal substances commonly employed act precisely through the pentose cycle, for example, the aforementioned hormones, cystostatic substances, antibiotics and antidiabetic sulfanilamide preparation. In this section we shall return to antibiotics, and we shall also discuss several groups of chemotherapeutic substances.

Besides the fact that some antibiotics enhance the process of glucose utilization through the pentose cycle, it is necessary to remember that a number of microorganisms receive their energy from glucose only or mainly through the pentose cycle. This problem was studied in general by De Ley who established that the species Aerobacterium Escherichia, Paracolobacterium, Serratia, Klebsiella, Salmonella, and Enterobacterialae utilize glucose mainly through the pentose cycle, whereas in the Proteus Erwinia species the pentose cycle plays a less important role. The literature in this respect is very extensive; we cite here at random several other species of microorganisms which contain pentose cycle enzymes: Corynebacterium creatovorans, Acetobacter suboxydans, Aspergillus niger, Sarcinallutea, Lactobacillus pentosus, Pseudomonas fluorescens, Sacharofila, B. subtilis, Propionibacterium pentosaceum, as well as yeast fungi (Torula utilis), etc.

The above is true also of viruses in cases where, depending on the type of virus, the metabolism of the affected host cells also undergoes change. It is possible that in some virus diseases a change takes place also in the manner of glucose splitting in the affected tissues.

Studies have been also carried to elicit the pentose cycle in parasites. It has been found that Tripanosoma rhodesiense has no enzymes (Grant). However, in insects (Musca domestica) the thoracid flying muscles utilize a complex pentose cycle, and the effect of some insecticides is precisely to block this cycle. Also, some fungicides (ethylenethiuram, for example) exert a specific inhibiting effect on the dehydrogenases of the pentose cycle (Chefurka).

We have been pursuing also the effect of largactyl on

the pentose cycle. It was elicited accidentally that in the erythrocytes of parturient women who had received this preparation there was a considerable diminution of the utilization of glucose by both methods (Stepanovský). We checked this effect later on rats (Kalouskovà). Some of the substances were tested only accidentally, but it is our opinion that it would be worthwhile to examine all substances which exert some influence on the metabolism, even if they seem to have no effect whatever on the metabolism of glycides. It would be expedient to clarify the effect of cytostatic, antihelminthic, deintoxicating, and antirheumatic substances, etc. It is possible that the effect of some of them is due precisely to the inhibition or activation of the pentose cycle, which manifests itself in changes in the concentrations of TPN, TPNH, SH-SS and other substances subsequently affecting the metabolism.

We must also mention the SH-substances that enter into the composition of some enzymes (and also TPN-dehydrogenases) and are found also in protoplasm in a free state. Their hydrogen is very mobile and, by virtue of the fact that they may be oxidized or reduced rapidly, they contribute to the maintenance of the redox potential. It is possible also that they participate in the transfer of hydrogen in certain oxidation processes. The SH-substances are very sensitive to certain "poisons" (heavy metals, for instance), while in an anaerobic medium they tend to become oxidized. In deoxidized form they are retained mainly by the pentose cycle dehydrogenases (Backer, Beutler), and possibly also by glucocorticoids (Wenner); conversely, they affect the pentose cycle by accelerating it.

The practical significance of SH-substances has grown in connection with a report that deoxidized SH-substances may be used as protection from ionizing radiation. The question arises as to whether the pentose cycle participates here in the deoxidation of SH-substances.

Vitamins

The relation of vitamins to the pentose cycle is of interest. Thiamine acts as a KO-transkelotase, and an accumulation of pentoses in the medium results (Huennekens). Also, L-ascorbic acid, which originates in connection with the pentose cycle, may itself influence the activity of the pentose cycle in tissues (through the correlation between ascorbic acid and dehydroascorbic acid). This fact explains the high concentration of Vitamin C in the suprarenal cortex observed concurrently with the high activity of the pentose cycle enzymes (see

also the section on CO_2 fixation).

Blood conservation

An erythrocyte cannot be regarded as a dead formation containing hemoglobin which transfers oxygen in a purely automatic way. An intact erythrocyte must, during the few months of its existence in media with different oncotic pressures, maintain its form and potassium level, prevent the penetration of sodium, renew its surface as it wears out mechanically, etc. In order to perform these tasks, the erythrocyte needs energy which it obtains via ambient splitting of glucose. Therefore in blood transfusions, the conserving fluids, which contain glucose, substantially prolong the life span of the erythrocytes introduced. Until now it was thought that the erythrocytes split the glucose by means of glycolysis, and thus the presence of dehydrogenases of the pentose cycle was considered to be of little practical significance. Recent reports that the addition of certain nucleotides substantially increases the storage period for conserved blood again stimulated interest in the pentose cycle of erythrocytes. It was discovered that "pirunriboside" /purinriboside?/ is split into purine and ribose-1-phosphate, the intermediate product of the pentose cycle (Huennekens). Another substantial proof was the discovery of methemoglobin reductase, an enzyme which transfers hydrogen from TPNH to methemoglobin, and thus regenerates hemoglobin. The sole producer of TPNH in erythrocytes is the pentose cycle; this means that the latter plays a part in enhancing the vitality of erythrocytes (James). Finally, it is noteworthy also that, thanks to TPNH, the erythrocytes are able to renew the lipids in their membranes. In examining new conserving mixtures, it will be necessary to test mainly those activators of the pentose cycle which transfer hydrogen, for example, methylene blue and SH-substances.

Pentosuria

Of independent significance is the so-called idiopathic pentosuria. Clinicians have devoted many reports to this disease, but the biochemical bases of this metabolic disturbance, which frequently affects whole families, have not been known until now. After time-consuming analyses, which often led to contradictory results, the conclusion has finally been reached that we are dealing, in a considerable number of pentosuria cases, with an L-xylulose (2-ketoxylose). This sugar originates, apparently, during the oxidation of D-glucuronic acid (Touster) or during the incomplete transformation of L-

xylulose into xylytol (Hollman), the intermediate stage between L- and D-xylulose; D-xylulose thus represents the normal metabolite of the pentose cycle.

Conclusion

Though the pentose cycle has been discovered comparatively recently, already a number of clinical problems connected with its presence are being formulated. Among these are (1) effect of ACTH on the pentose cycle and hydrocortisone synthesis; (2) the activating effect of thyoxin on the pentose cycle and the effect of the latter on cholesterin biosynthesis; (4) the regulating effect of the pentose cycle on the biosynthesis of fats; (5) the relation of the pentose cycle to microorganisms, infections and antibiotics, fungicides and insecticides; (6) the effect of certain chemo-therapeutic substances (ganglioplegic) on the activity of the pentose cycle; (7) the pentose cycle and ionizing radiation; (8) the pentose cycle and blood conservation; (9) pentosuria; (10) photosynthesis in plants.

The aforementioned problems are, in the majority of cases, in the stage of initial study and will require systematic investigation. We do not recommend the use of radio isotopes in clinical studies on human erythrocytes.

Appendix

The study of the pentose cycle, which until recently had been the exclusive concern of biochemists, was carried out on tissue homogenates (at first on rat liver homogenates), as well as via administration of labeled glucose or its derivatives to rats. The correlation of the data obtained with medical data has met with methodological difficulties. True, hepatologists (E. Schmidt and F. Schmidt) are trying to ascertain the activity of pentose cycle enzymes in liver punctates in their patients, but this method of obtaining material for enzymic study is unfit for general use in practice; still more difficulties would be encountered in the use of this method for the study of changes in pentose cycle activity over brief periods of time, for example, after certain stresses (administration of glucose, hormones, etc.). The study available biochemical materials (urine or serum) did not appear promising to us nevertheless, in 1953 we began studying the pentose cycle in humans after having discovered accidentally an increased quantity of pentoses in the urine of individuals who had been given ACTH (Sonka). However, taking into account the difficulty of standardizing the concentration of the urine and the elimination of sugars and enzymes, we gave up searching

for a method based only on urine analysis.

Menkes and Peleman demonstrated that the blood serum of cancer patients splits ribose and some other pentoses abnormally rapidly (although they were not aware of the existence of the pentose cycle and attempted to utilize these facts for the diagnosis of malignant tumors). Their works were subjected to criticism, and it was pointed out that not all cancer patients have a pronounced pentolysis and that therefore this could not be used as a test (Kubovitz, Roe). Menkes and his critics, in their search for a reliable "diagnostic test" for cancer, did not notice the true significance of the existence of a more active pentose cycle in cancer patients.

In view of the aforementioned methodological difficulties, we turned to the study of erythrocytes in regard to which, in addition to anaerobic glycolysis, the presence of certain enzymes of the pentose cycle has already been proved (Bruns,Warburg). It is necessary to point out that anaerobic glycolysis in the erythrocytes terminates with accumulation of 2,3-diphosphopyruvate and lactate (Gousley); in this connection, only certain vestigial enzymes of the citric acid cycle remains in mature erythrocytes (Spicer). The possibility is not excluded that erythrocytes contain only enzymes of the gliooxylate cycle (V. A. Engel'gardt).

In the course of time we established the following recommended working method, the details of which have been published (Kalousek, Palek). Venous blood is collected in test tubes treated with heparin. Following centrifugation, the plasma and upper layer of leucocytes are removed. The erythrocytes then are washed twice in a phosphate buffer (pH 7.4) with a physiological solution and, after centrifugation, the upper erythrocyte layer is removed. After this, one ml of the erythrocyte suspension (hematocrit 80) is incubated in a washing solution to which glucose is added up to a concentration of 120 mg-percent. From part of this suspension the proteins of trichloracetic acid are removed immediately, while the other part, after vigorous shaking (saturation with oxygen), is incubated in a thermostat at 37° for three hours, after which the proteins are removed by the same method.

We extracted phospho-sugar for 12 hours at a temperature of one degree, and then determined the decrease in glucose and increase in ribose contents in the incubated and the control specimens by means of the Bial reaction as modified by Meybaumova; then we measured the absorption maximum on the Coleman Gun spetrophotometer at wavelengths of 540 m and 680 m. We eliminated the possible coincidence of both stained

complexes by means of Knudson's equation with two unknowns. On the basis of the data thus obtained, we calculated the coefficient $\frac{R}{G} \times 100$ (R quantity of ribose formed G quantity of glucose metabolized in one ml of incubated erythrocyte suspension during a three hour period; both quantities are expressed in micromoles). The figures obtained corresponded with the data of other authors in regard to the percentage activity of the pentose cycle in the rat liver homogenates and sections and in certain other tissues, and in the utilization of C^{14}-labeled phosphorylated derivatives of glucose, on the first, second and sixth carbon of the glucose molecule (Ashmore, Wenner).

Finally, in the studies carried out with human erythrocytes, in which tagged atoms were employed, results were cited for the pentose cycle and anaerobic glycolysis which proved to be identical with our data (G. A. Kritskiy). Our method enabled us to carry out a complex clinical study of the regulating mechanism of the pentose cycle on repeated, even serial, specimens of metabolically active tissues in the same individuals, although we were aware that the erythrocytes differ somewhat in their metabolism from hepatic or muscular cells, for instance, in the method of penetration of glucose into the cells.

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